MAIL STOP
APPEAL BRIEF - PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	J. Rine et al.	Attorney Docket No.:	UOCB118456
Application No.:	10/038,206	Art Unit: 1631 / Confirmation No.:	1317
Filed:	January 2, 2002	Examiner:	J.S. Brusca
Title:	SYSTEMS FOR GENERATING AND ANALYZING STIMULUS-RESPONSE OUTPUT SIGNAL MATRICES		

RESPONSE TO NOTIFICATION OF
NON-COMPLIANT APPEAL BRIEF (37 C.F.R. 41.37)

Seattle, Washington 98101

December 15, 2005

TO THE COMMISSIONER FOR PATENTS:

This paper is filed in reply to the Notification of Non-compliant Appeal Brief dated November 28, 2005. A Revised Appeal Brief is attached.

With regard to Item 4, the Examiner indicates that the brief does not contain a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number and to the drawings. Applicants have revised Section V in the Revised Appeal Brief, attached herewith, to include references to the specification.

With regard to Item 10, the Examiner also indicated that the Status of Amendments section fails to note that no amendments were submitted after final rejection. Applicants have revised Section IV to include the statement that no claim amendments were submitted after the final rejection.

Applicants apologize for any inconvenience the foregoing may have caused the Office.

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If the Examiner has any further questions or comments, he is invited to call applicants' attorney at the number listed below. Otherwise, it is believed that the Revised Appeal Brief conforms to the new appeal rules as set forth in 37 C.F.R. 41.37.

Respectfully submitted,

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Date: December 19, 2005

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BRIEF - PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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APPELLANTS' APPEAL BRIEF

Seattle, Washington
December 15, 2005

TO THE COMMISSIONER FOR PATENTS:

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I. REAL PARTY IN INTEREST

Regents of the University of California, a California non-profit organization, having a place of business at 300 Lakeside Drive, 22nd Floor, Oakland, California 94612, is the assignee of the entire interest of the appealed subject matter.

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II. RELATED APPEALS AND INTERFERENCES

There are none.

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III. STATUS OF CLAIMS

Claims 38-85 are pending in the application. All stand rejected under 35 U.S.C. § 103(a). Claims 38-85 are appealed. The table below indicates their status.

Claim(s)	Status	Appealed
1-37	Canceled	No
38	Rejected	Yes
39	Rejected	Yes
40	Rejected	Yes
41	Rejected	Yes
42	Rejected	Yes
43	Rejected	Yes
44	Rejected	Yes
45	Rejected	Yes
46	Rejected	Yes
47	Rejected	Yes
48	Rejected	Yes
49	Rejected	Yes
50	Rejected	Yes
51	Rejected	Yes
52	Rejected	Yes
53	Rejected	Yes
54	Rejected	Yes
55	Rejected	Yes
56	Rejected	Yes
57	Rejected	Yes
58	Rejected	Yes
59	Rejected	Yes
60	Rejected	Yes
61	Rejected	Yes
62	Rejected	Yes
63	Rejected	Yes
64	Rejected	Yes
65	Rejected	Yes
66	Rejected	Yes
67	Rejected	Yes
68	Rejected	Yes
69	Rejected	Yes

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Claim(s)	Status	Appealed
70	Rejected	Yes
71	Rejected	Yes
72	Rejected	Yes
73	Rejected	Yes
74	Rejected	Yes
75	Rejected	Yes
76	Rejected	Yes
77	Rejected	Yes
78	Rejected	Yes
79	Rejected	Yes
80	Rejected	Yes
81	Rejected	Yes
82	Rejected	Yes
83	Rejected	Yes
84	Rejected	Yes
85	Rejected	Yes

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IV. STATUS OF AMENDMENTS

The application was rejected in an Office Action dated August 20, 2004. Thereafter an Amendment and Response to the non-final Office Action was mailed on February 4, 2005, and entered into the file. The application was finally rejected in a paper dated April 6, 2005. No claims amendments were submitted after the final rejection. A copy of the claims, as amended, is attached in the Claims Appendix.

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V. SUMMARY OF CLAIMED SUBJECT MATTER

There are three independent claims on appeal, Claims 38, 56, and 70. Claim 38 is directed to a method for analyzing the effects of subjecting a living thing to a stimulus. In the practice of the method, physical signals are detected from a plurality of units ordered in a probe matrix. (Specification, page 5, line 28, to page 6, line 12, FIGURE 2.) Each unit of the plurality of units confines a probe (e.g., a DNA molecule) comprising a pre-determined sequence of nucleotides. (Specification, page 5, lines 15-25.) Each of the pre-determined sequences is hybridizable with a different identified gene (or transcript thereof, or cDNA derived therefrom) of the living thing. (Specification, page 8, line 17, to page 9, line 1.) The probe matrix is contacted with gene transcripts or cDNA derived from the living thing subjected to the stimulus, and the resulting physical signals are transduced into electrical output signals. (Specification, page 5, line 28, to page 6, line 17, FIGURE 2, FIGURE 4.) Each electrical output signal is stored in digital form in an output signal data structure, wherein each stored digital signal is associated (i) with the stimulus and (ii) with the identity of the identified gene. (Specification, page 6, line 22, to page 7, line 8; page 13, line 28, to page 14, line 13; FIGURE 1, FIGURE 2.) The effect of the stimulus on the living thing is analyzed by comparing the stored output signal data structure with an output signal data structure database, wherein the output signal data structure database comprises a plurality of output signal data structures stored in a computer memory. (Specification, page 7, lines 8 to 30; FIGURE 5.)

Claim 56 is directed to a method for producing an output signal data structure database recording the effect of subjecting a living thing to a plurality of stimuli. In the practice of the method, physical signals are detected from a plurality of units ordered in a probe matrix. (Specification, page 5, line 28, to page 6, line 12; FIGURE 2.) Each unit of the plurality of units confines a probe (e.g., a DNA molecule) comprising a pre-determined sequence of nucleotides. (Specification, page 5, lines 15-25.) Each of the pre-determined sequences is hybridizable with a different identified gene (or transcript thereof, or cDNA derived therefrom) of the living thing. (Specification, page 8, line 17, to page 9, line 1.) The probe matrix is contacted with gene transcripts or cDNA derived from the living thing subjected to the stimulus, and the resulting physical signals are transduced into electrical output signals. (Specification, page 5, line 28, to page 6, line 17; FIGURE 2, FIGURE 4.) Each electrical output signal is stored in digital form in an output signal data structure, wherein each stored digital signal is associated (i) with the stimulus and (ii) with the identity of the identified gene. (Specification, page 6, line 22, to

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page 7, line 8; page 13, line 28, to page 14, line 13; FIGURE 1, FIGURE 2.) The steps of detecting, transducing, and storing for a plurality of stimuli are repeated to form an output signal data structure database. (Specification, page 13, line 28, to page 14, line 20.)

Claim 70 is directed to a method for determining a response profile for a stimulus. Physical signals are detected from a plurality of units ordered in a probe matrix by contacting the probe matrix with gene transcripts or cDNA derived from the living thing subjected to the stimulus. (Specification, page 5, line 28, to page 6, line 12, FIGURE 2.) Each unit of the plurality of units confines a probe comprising a pre-determined sequence of nucleotides, and each of the pre-determined sequences is hybridizable with a different identified gene of the living thing, or with a transcript of the gene, or with cDNA derived from the gene. (Specification, page 5, lines 15-25, page 8, line 17, to page 9, line 1.) The physical signals are transduced into electrical output signals and stored in digital form in a stimulus response data structure, wherein each stored digital signal is associated (i) with the stimulus and (ii) with the identity of the identified gene. (Specification, page 5, line 28, to page 6, line 17; FIGURE 2, FIGURE 4; page 6, line 22, to page 7, line 8; page 13, line 28, to page 14, line 13; FIGURE 1, FIGURE 2.) A response profile for the stimulus is determined by comparing the stimulus response data structure with a basal response data structure produced by carrying out the foregoing steps of detecting, transducing, and storing, except that the probe matrix contacted with gene transcripts or cDNA derived from the living thing is subjected to basal conditions. (Specification, page 14, line 21, to page 17, line 5; FIGURE 6, FIGURE 7.)

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VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

First Ground of Rejection - Claim 69

Claim 69 is rejected under 35 U.S.C. § 101 because the Examiner argues that the claimed invention is directed to non-statutory subject matter. The Examiner argues that Claim 69 is drawn to data and computer readable memory which is not patentable subject matter.

Second Ground of Rejection - Claims 38-53, 55-66, 68-83, and 85

Claims 38-53, 55-66, 68-83, and 85 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gress et al. (*Mammalian Genome 3*:609-619 (1992)), in view of Granelli-Piperno et al. (*J. Exp. Med. 163*:922-937, 1986), in view of Fodor et al. (U.S. Patent No. 5,800,992).

Third Ground of Rejection - Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84

Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gress et al., in view of Granelli-Piperno et al., in view of Fodor et al., as applied to Claims 38-53, 55-66, 68-83, and 85 above, and further in view of Watson et al. (*Molecular Biology of the Gene*, 4th ed., Benjamin Cummings, Menlo Park, 1987, pp. 550-594).

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VII. ARGUMENT

Rejection Under 35 U.S.C. § 101

Claim 69

Claim 69 is rejected under 35 U.S.C. § 101 because the Examiner argues that the claimed invention is directed to non-statutory subject matter. The Examiner argues that Claim 69 is drawn to data and computer-readable memory which is not patentable subject matter (*citing* Manual of Patent Examining Procedure (hereinafter M.P.E.P.) § 2106).

Applicants submit that Claim 69 is directed to a computer memory (i.e., a computer-readable medium) storing an output signal data structure database produced by the method of Claim 56.

It is well established that functional descriptive material recorded on a computer-readable memory is patentable ("When functional descriptive material is recorded on some computer readable medium (e.g., a computer memory) it becomes structurally and functionally interrelated to the medium and will be statutory in most cases since use of technology permits the function of the descriptive material to be realized." M.P.E.P. § 2106(IV)(B)(1), citing *In re Lowry*, 32 U.S.P.Q.2d 1031, 1035 (Fed. Cir. 1994)).

A definition of functional descriptive material is provided in M.P.E.P. § 2106(IV)(B)(1):

> Functional descriptive material consists of data structures and computer programs which impart functionality when employed as a computer component. (The definition of "data structure" is "a physical or logical relationship among data elements, designed to support specific data manipulation functions.")

The material stored in the computer memory encompassed by Claim 69 includes a data structure database wherein stored digital signals are associated with (I) a stimulus and (II) the identity of an identified gene. This stored information imparts the function of permitting a user to associate a stimulus with the identity of an identified gene, and to use that information and association to gain insights into the function of biological cells and organisms. Thus, applicants submit that the information stored in the computer memory is functional descriptive material recorded on a computer-readable memory, and so is patentable subject matter.

Additionally, M.P.E.P. § 2106(IV)(B)(1)(a) at page 2100-13 (Col. 2) states, "When a computer program is recited in conjunction with a physical structure, such as a computer memory, Office personnel should treat the claim as a product claim."

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In this regard, Claim 69 recites that a comparison function, of a computer comprising the computer memory, compares an output signal matrix with the output signal data structure database to deduce characteristics of a stimulus applied to a living thing. Thus, Claim 69 recites a computer program (the comparison function of Claim 69) in conjunction with a computer memory. Accordingly, applicants submit that Claim 69 should be treated as a product claim that defines patentable subject matter.

For the foregoing reasons, applicants respectfully request withdrawal of the rejection of Claim 69 under 35 U.S.C. § 101.

Rejections Under 35 U.S.C. § 103(a)

Claims 38-53, 55-66, 68-83, and 85

Claims 38-53, 55-66, 68-83, and 85 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gress et al., in view of Granelli-Piperno et al., in view of Fodor et al.

The Examiner's Proposed Modification Renders the Gress et al. Method Unsatisfactory for its Intended Purpose: It is well established that if a proposed modification would render a prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *See, In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984).

Gress et al. discloses a method for characterizing large numbers of cDNA library clones, and is useful, for example, to identify cDNA clones that are abundantly expressed in several tissues, and that are likely to encode proteins involved in structural and regulatory functions in every cell. The identified cDNA clones can then be partially sequenced, so as to allow the correlation of genomic mapping, transcriptional and sequence information into a global data set (see Gress et al. at page 609, Col. 1, last two sentences, and Col. 2, first paragraph, last sentence; page 610, Col. 1, second paragraph, last sentence). In the practice of the Gress et al. method, thousands of unidentified cDNA clones from human fetal brain, and from *Drosophila* embryos, are arrayed on a nitrocellulose filter, and hybridized against a labeled cDNA pool derived from mouse tissues. Partial sequence data for clones of interest are then generated (see Gress et al. at sentence spanning pages 617-618). (Only a small number of *Drosophila* cDNA clones were sequenced in Gress et al. in order to demonstrate the applicability of the approach to the *Drosophila* genome; see Gress et al. at page 613, Col. 2, 1st paragraph.)

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The Examiner argues that it would have been obvious to modify the method of Gress et al. by using an array of probes which each have a pre-determined sequence as disclosed by Fodor et al., because Fodor et al. shows that such an array has the advantage of allowing the sequences detected in the sample to be mapped to a particular location of the genome of the organism sampled. The Examiner further argues that Gress et al. sequence selected clones to facilitate correlation of their results with other databases as shown in the abstract of Gress et al., and so it is therefore apparent that the prior art shows advantages and motivation for determining the sequence of elements of an array. The Examiner also argues that Fodor et al. has been cited to show that the prior art details a method to create an array with predetermined sequences at each element, which has the advantage of obviating subsequent sequencing to characterize elements of interest determined by the hybridization experiment.

Applicants submit that the Examiner's proposal to replace the thousands of unidentified cDNA clones that are arrayed on a nitrocellulose filter, or other substrate, as taught by Gress et al., with oligonucleotides having known sequences, would render the Gress et al. invention inoperable for its intended purpose. For example, in the Gress et al. publication thousands of unidentified cDNA clones from human fetal brain, and from *Drosophila* embryos, are arrayed on a nitrocellulose filter, and hybridized against a labeled cDNA pool derived from mouse tissues. The strongly hybridizing clones are selected for sequencing because these are likely to encode highly expressed proteins that are involved in structural and regulatory functions in every cell, and which are conserved throughout a wide range of species. The successful practice of the Gress et al. method does not require any knowledge of the identity or sequence of the cDNA clones that are being sought. Indeed, it would be nonsensical to use probes of known sequence in order to determine which of the probes of known sequence will be sequenced.

Moreover, modification of the Gress et al. invention to replace the thousands of unidentified cDNA clones arrayed on a substrate with thousands of probes which each have a pre-determined sequence, as suggested by the Examiner, would only permit an investigator to identify the expression pattern of those clones in the pool that happen to hybridize to one of the pre-determined sequences. Clones that do not hybridize to one of the pre-determined sequences could not be screened using the modified method of Gress et al. Even if the pre-determined sequences were selected to hybridize to thousands of different expressed genes (or cDNAs derived therefrom), one of ordinary skill in the art would have to know at least part of the sequence of each of the thousands of different expressed genes (or cDNAs derived therefrom).

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Consequently, applicants submit that it is not obvious to modify the Gress et al. method by incorporating the teachings of the Fodor et al. publication as suggested by the Examiner. Moreover, the Granelli-Piperno et al. publication, cited by the Examiner, does not cure the deficiencies of Gress et al., since it does not teach a plurality of units, ordered in a probe matrix, each of which confines a probe comprising a pre-determined nucleotide sequence.

Moreover, particularly regarding Claims 49-51, as well as Claims 63-65, and Claims 80-82, Granelli-Piperno, alone or in combination with the other references, does not render obvious these claims because Granelli-Piperno only teaches studying the effect of the stimulus on the expression of a small subset of genes in a cell. Granelli-Piperno is interested in analyzing the control of lymphokine mRNA levels (see page 922, third full paragraph), and thus looks at the levels of mRNAs of nine different genes in stimulated T cells (see paragraph spanning pages 924-925). In contrast, each of the aforementioned set of claims specify that the probe matrix comprises probes having sequences that are hybridizable with at least 0.5%, 5%, or 50%, respectively, of the genes of the living thing (or with transcripts of at least 0.5%, 5%, or 50%, respectively, of the genes, or with the cDNA derived from at least 0.5%, 5%, or 50%, respectively of the genes). Thus, these claims are nonobvious for this additional reason.

Gress et al. teaches away from sequencing array elements: In the Office Action mailed August 20, 2004, the Examiner further argues that Gress et al. does not teach away from sequenced array elements. The Examiner states that Gress et al. does not sequence all array elements in order to reduce labor involved in sequencing those elements that do not hybridize to probes of interest and are therefore elements that are not of interest. In the Office Action mailed April 6, 2005, the Examiner argues that Gress et al. does sequence selected clones to facilitate correlation of their results with other databases as shown in the abstract of Gress et al. The Examiner concludes that it is therefore apparent that the prior art shows advantages and motivation for determining the sequence of elements of an array.

Applicants submit that Gress et al. did not sequence all the array elements because the use of sequenced array elements is not necessary for the successful use of the Gress et al. invention. Consequently, as described more fully herein, applicants submit that there is no motivation to modify the Gress et al. invention to incorporate sequenced array elements, because the use of sequenced array elements is not necessary for the successful use of the Gress et al. invention, and one of ordinary skill in the art would not be motivated to expend considerable time and money unnecessarily sequencing thousands of array elements.

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In order to use an array of sequenced cDNA molecules in the practice of the Gress et al. method, the thousands of cDNA molecules that are to be arrayed on a substrate would first have to be sequenced. An array of cDNA-specific oligonucleotide hybridization probes could be used instead of the corresponding cDNAs, but each of the thousands of cDNA molecules would have to be sufficiently sequenced to identify an oligonucleotide sequence element that is unique to each cDNA, and that acts as a cDNA-specific hybridization probe under defined hybridization conditions. Sequencing the thousands of cDNAs arrayed on a substrate in the practice of the Gress et al. invention would be very tedious and time-consuming and, more importantly, is unnecessary. Accordingly, applicants submit that one of ordinary skill in the art would not be motivated to modify the Gress et al. invention to use sequenced array elements instead of unsequenced array elements.

Applicant Submits That the Examiner is Impermissibly Engaging in Hindsight Analysis by Combining Elements From Gress et al. and Fodor et al.: It is well established that prior art references must be read as a whole and consideration must be given where the references diverge and teach away from the claimed invention. It is impermissible to pick and choose among individual parts of assorted prior art references to recreate the claimed invention. *See*, e.g., *Azko N.V. v. United States Int'l Trade Comm'n*, 808 F.2d 1471, 1481, 1 U.S.P.Q.2d 1241, 1246 (Fed. Cir. 1986), *cert. denied*, 107 S.Ct. 2490 (1987).

In the present case, the Examiner relies upon Gress et al. as disclosing a general method of assaying patterns of transcription by use of labeled cDNA from mouse and human cells by use of a cDNA X-Y coordinate grid array of probes. The Examiner characterizes Fodor et al. as showing throughout a method of making an array of polynucleotide probes of predetermined sequence by independent *in situ* stepwise synthesis of each oligonucleotide probe from the array.

Applicants submit that the Examiner does not give due consideration to where the references diverge and teach away from the claimed invention. Thus, for example, applicants submit that the Examiner does not give due weight to the fact that Gress et al. teaches screening thousands of unidentified cDNA clones, using an array of cDNA probes, in order to identify the most highly expressed clones, without biasing the result by selecting certain groups of clones that hybridize to probes having defined sequences. In contrast, Fodor et al. is concerned with the manufacture and use of arrays of probes having defined sequences that can be used to measure the level of expression of specific populations of nucleic acid molecules. Applicants submit that the purpose and focus of the Gress et al. and Fodor et al. publications are quite different, and that

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when the two publications are each read as a whole, there is no motivation to combine them, or to select individual elements of the disclosure of each of these publications and combine them.

In view of the foregoing arguments, applicants submit that Claims 38-53, 55-66, 68-83, and 85 are not obvious in view of Gress et al., in view of Granelli-Piperno et al., in view of Fodor et al. Applicants respectfully request that the rejection of Claims 38-53, 55-66, 68-83, and 85 under 35 U.S.C. § 103(a) be withdrawn.

Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84

Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gress et al., in view of Granelli-Piperno et al., in view of Fodor et al., as applied to Claims 38-53, 55-66, 68-83, and 85, and further in view of Watson et al.

The Examiner characterizes the rejected claims as being drawn to assays utilizing fungal cells, and cites Watson et al., pp. 573-575, for its teaching that these cells contain genes that are regulated by stimuli such as metabolites.

For the reasons set forth in connection with the rejection of Claims 38-53, 55-66, 68-83, and 85 under 35 U.S.C. § 103(a), applicants submit that it is not obvious to combine the teachings of Gress et al. and Fodor et al., as suggested by the Examiner. This deficiency is not cured by the teachings of either Granelli-Piperno et al. or Watson et al. Applicants respectfully request that the rejection of Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 under 35 U.S.C. § 103(a) be withdrawn.

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Date: December 19, 2005

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VIII. CLAIMS APPENDIX

1-37. (Canceled)

38. A method for analyzing the effects of subjecting a living thing to a stimulus comprising:

(a) detecting physical signals from a plurality of units ordered in a probe matrix by contacting the probe matrix with gene transcripts or cDNA derived from said living thing subjected to said stimulus, wherein each unit of the plurality of units confines a probe comprising a pre-determined sequence of nucleotides, and wherein each of said pre-determined sequences is hybridizable with a different identified gene of said living thing, or with a transcript of the gene, or with cDNA derived from the gene,

(b) transducing the physical signals into electrical output signals,

(c) storing in digital form each electrical output signal in an output signal data structure, wherein each stored digital signal is associated (i) with said stimulus and (ii) with the identity of said identified gene, and

(d) analyzing the effect of said stimulus on said living thing by comparing the stored output signal data structure with an output signal data structure database, wherein the output signal data structure database comprises a plurality of output signal data structures stored in a computer memory.

39. The method of claim 38 wherein the probes are 24-240 nucleotides in length.

40. The method of claim 38 wherein the probes comprise lengths of nucleotide sequences selected so as to be hybridizable with a transcript or cDNA derived from said identified gene.

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41. The method of claim 38 wherein the probes comprise polynucleotide sequences not hybridizable to more than one contiguous gene of the living thing.

42. The method of claim 38 wherein the gene transcripts or cDNA derived from the living thing are labeled.

43. The method of claim 38 wherein the ordered units in a probe matrix comprise an ordered array of units identified by X and Y coordinates, and wherein output signal data structures comprise matrices with elements identified by the X and Y coordinates.

44. The method of claim 43 further comprising establishing a table relating the X and Y coordinates of each unit to the identity of said identified gene.

45. The method of claim 38 wherein the step of storing further comprises storing each digital signal in a computer readable memory.

46. The method of claim 38 wherein the probe matrix comprises oligonucleotide probes that are arrayed on a substrate.

47. The method of claim 38 further comprising a step of producing the output signal data structure database by a method comprising:

(a) detecting physical signals from a plurality of units ordered in a probe matrix by contacting the probe matrix with gene transcripts or cDNA derived from said living thing subjected to a stimulus, wherein each unit of the plurality of units confines a probe comprising a pre-determined sequence of nucleotides, and wherein each of said pre-determined sequences is hybridizable with a different identified gene of said living thing, or with a transcript of the gene, or with cDNA derived from the gene,

(b) transducing the physical signals into electrical output signals,

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(c) storing in digital form each electrical output signal in an output signal data structure, wherein each stored digital signal is associated (i) with said stimulus and (ii) with the identity of said identified gene, and

(d) repeating steps of detecting, transducing, and storing for a plurality of stimuli to form an output signal data structure database.

48. The method of claim 47 wherein the probes comprise polynucleotide sequences not hybridizable to more than one contiguous gene of the living thing.

49. The method of claim 38 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 0.5% of the genes of said living thing, or with transcripts of at least 0.5% of said genes, or with the cDNA derived from at least 0.5% of said genes.

50. The method of claim 49 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 5% of the genes of said living thing, or with transcripts of at least 5% of said genes, or with the cDNA derived from at least 5% of said genes.

51. The method of claim 50 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 50% of the genes of said living thing, or with transcripts of at least 50% of said genes, or with the cDNA derived from at least 50% of said genes.

52. The method of claim 38 wherein the probe matrix comprises probes having sequences that are hybridizable with a functional class or subset of the genes of said living thing, or with transcripts of the functional class or subset of said genes, or with the cDNA derived from the functional class or subset of said genes.

53. The method of claim 49, 50 or 51 wherein the living thing is a human.

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54. The method of claim 49, 50 or 51 wherein the living thing is a fungus.

55. The method of claim 49, 50 or 51 wherein the living thing is a eukaryote.

56. A method for producing an output signal data structure database recording the effect of subjecting a living thing to a plurality of stimuli comprising:

(a) detecting physical signals from a plurality of units ordered in a probe matrix by contacting the probe matrix with gene transcripts or cDNA derived from said living thing subjected to said stimulus, wherein each unit of the plurality of units confines a probe comprising a pre-determined sequence of nucleotides, and wherein each of said pre-determined sequences is hybridizable with a different identified gene of said living thing, or with a transcript of the gene, or with cDNA derived from the gene,

(b) transducing the physical signals into electrical output signals,

(c) storing in digital form each electrical output signal in an output signal data structure, wherein each stored digital signal is associated (i) with said stimulus and (ii) with the identity of said identified gene, and

(d) repeating steps of detecting, transducing, and storing for a plurality of stimuli to form an output signal data structure database.

57. The method of claim 56 wherein the stimuli comprise basal conditions.

58. The method of claim 56 wherein the probes are 24-240 nucleotides in length.

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59. The method of claim 56 wherein the probes comprise nucleotide sequences selected so as to be hybridizable with a transcript of one or more of the identified genes, or with cDNA derived from one or more of the identified genes.

60. The method of claim 56 wherein the gene transcripts or cDNA derived from the living thing are labeled.

61. The method of claim 56 wherein the polynucleotide sequence of each probe is not hybridizable to more than one contiguous gene of the living thing.

62. The method of claim 56 wherein the ordered units in a probe matrix comprise an ordered array of units identified by X and Y coordinates, and wherein output signal data structures comprise matrices with elements identified by the X and Y coordinates.

63. The method of claim 56 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 0.5% of the genes of said living thing, or with transcripts of at least 0.5% of said genes, or with the cDNA derived from at least 0.5% of said genes.

64. The method of claim 63 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 5% of the genes of said living thing, or with transcripts of at least 5% of said genes, or with the cDNA derived from at least 5% of said genes.

65. The method of claim 64 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 50% of the genes of said living thing, or with transcripts of at least 50% of said genes, or with the cDNA derived from at least 50% of said genes.

66. The method of claim 63, 64 or 65 wherein the living thing is a human.

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67. The method of claim 63, 64 or 65 wherein the living thing is a fungus.

68. The method of claim 63, 64 or 65 wherein the living thing is a eukaryote.

69. A computer memory storing an output signal data structure database produced by the method of claim 56, wherein a comparison function of a computer comprising the computer memory compares an output signal matrix with the output signal data structure database to deduce characteristics of a stimulus applied to a living thing.

70. A method for determining a response profile for a stimulus comprising:

(a) detecting physical signals from a plurality of units ordered in a probe matrix by contacting the probe matrix with gene transcripts or cDNA derived from said living thing subjected to said stimulus, wherein each unit of the plurality of units confines a probe comprising a pre-determined sequence of nucleotides, and wherein each of said pre-determined sequences is hybridizable with a different identified gene of said living thing, or with a transcript of the gene, or with cDNA derived from the gene,

(b) transducing the physical signals into electrical output signals,

(c) storing in digital form each electrical output signal in a stimulus response data structure, wherein each stored digital signal is associated (i) with said stimulus and (ii) with the identity of said identified gene, and

(d) determining a response profile for the stimulus by comparing the stimulus response data structure with a basal response data structure produced by carrying out the steps of detecting, transducing, and storing as above except that the probe matrix contacted with gene transcripts or cDNA derived from said living thing is subjected to basal conditions.

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71. The method of claim 70 wherein the step of comparing comprises subtracting the elements of the stimulus response data structure and the basal response data structure.

72. The method of claim 70 wherein the step of comparing comprises dividing the elements of the stimulus response data structure and the basal response data structure.

73. The method of claim 70 wherein the probes are 24-240 nucleotides in length.

74. The method of claim 70 wherein the probes comprise lengths of nucleotide sequences selected so as to be hybridizable with a transcript or cDNA derived from a identified gene.

75. The method of claim 70 wherein the probes comprise polynucleotide sequences not hybridizable to more than one contiguous gene of the living thing.

76. The method of claim 70 wherein the gene transcripts or cDNA derived from the living thing are labeled.

77. The method of claim 70 wherein the ordered units in a probe matrix comprise an ordered array of units identified by X and Y coordinates, and wherein output signal data structures comprise matrices with elements identified by the X and Y coordinates.

78. The method of claim 70 wherein the step of storing further comprises storing each digital signal in a computer readable memory

79. The method of claim 70 wherein the probe matrix comprises oligonucleotide probes that are arrayed on a substrate.

80. The method of claim 70 wherein the probe matrix comprises probes having sequences that are hybridizable with at least

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0.5% of the genes of said living thing, or with transcripts of at least 0.5% of said genes, or with the cDNA derived from at least 0.5% of said genes.

81. The method of claim 80 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 5% of the genes of said living thing, or with transcripts of at least 5% of said genes, or with the cDNA derived from at least 5% of said genes.

82. The method of claim 81 wherein the probe matrix comprises probes having sequences that are hybridizable with at least 50% of the genes of said living thing, or with transcripts of at least 50% of said genes, or with the cDNA derived from at least 50% of said genes.

83. The method of claim 80, 81 or 82 wherein the living thing is a human.

84. The method of claim 80, 81 or 82 wherein the living thing is a fungus.

85. The method of claim 80, 81 or 82 wherein the living thing is a eukaryote.

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IX. EVIDENCE APPENDIX

None.

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X. RELATED PROCEEDINGS APPENDIX

None.

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